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"Stressed" About Air Pollution:

Time for Personal Action

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Keywords

Editorials

The modern era has borne witness to a dramatic shift in the global burden of disease toward noncommunicable illnesses associated with economic affluence (eg, diabetes mellitus, heart diseases).[1] Although primeval problems menacing humanity since the dawn of time such as undernutrition/famine, unsafe drinking water, and infectious diseases persist (and may worsen in the future as a result of climate change), their relative importance has been considerably reduced during the past half-century.[1,2] In contrast, anthropogenic ambient air pollution (mainly particulate matter <2.5 μm [$PM_{2.5}$]) remains a recalcitrant and growing threat to global health and well-being. As of 2015, exposure to ambient $PM_{2.5}$ ranked fifth—closely following hypertension, smoking, high glucose, and elevated cholesterol, respectively—as a leading global risk factor for morbidity and mortality. [2] $PM_{2.5}$ promotes many illnesses, including cancer and lung disease. However, the greatest portion of death and disability is from cardiovascular events (myocardial infarction, stroke, heart failure), and, as such, air pollution has been formally recognized by both the American Heart Association and European Society of Cardiology as an independent risk factor.[3,4]

Most recent estimates are that 4.2 million deaths (7.6% of total global mortality and 700 000 more deaths in 2015 compared with 1990)[2] are attributable to ambient $PM_{2.5}$. Cardiovascular diseases account for ≈57% of these deaths, with South and East Asia contributing ≈60% of total $PM_{2.5}$-related mortality. Despite substantial improvements in air quality throughout much of North America, the population-weighted $PM_{2.5}$ exposure has increased worldwide from 1990 (39.7 $\mu g/m^3$) to 2015 (44.2 $\mu g/m^3$).[2] This increase was largely because of a worsening of air quality and population growth across Asia, Africa, and the Middle East. These facts paint a stark picture highlighting the clear and present danger

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FOOTNOTES

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posed by air pollution. First, forecasted demographic and epidemiological transitions in India and China, along with other rapidly developing economies, imply that a business-as-usual strategy is not tenable. Aiming to simply continue the status quo, already resulting in unacceptably high mortality rates from $PM_{2.5}$, would require a 20% to 30% decline in levels over the next 15 years just to offset the negative influence attributable to the anticipated growth of the susceptible (aging) population. Second, the supralinear nature of the integrated exposure-response function of $PM_{2.5}$ (steeper at lower compared with higher concentrations) dictates that for a given decrease in air pollution, reductions in per-capita mortality will likely be paradoxically greater in economies with preexisting good compared with poorer air quality. Considerable positive impact on global mortality can be accomplished through aggressive national policies to improve air quality in India and China (population-weighted mean $PM_{2.5}$ exposure levels of 74.3 and 58.4 $\mu g/m^3$, respectively), which together account for >50% of global $PM_{2.5}$ mortality.[2] However, substantial public health benefits can still accrue from taking additional actions to provide further reductions in ambient $PM_{2.5}$ levels even in comparatively clean countries. This includes the United States (population-weighted mean $PM_{2.5}$ exposure level of 8.4 $\mu g/m^3$),[2] where the public has already enjoyed an increase in life expectancy since 1980 from improved air quality.[5] Indeed, mounting evidence supports that no threshold exists below which $PM_{2.5}$ no longer poses a health risk to the population, even when levels are within annual World Health Organization Air Quality Guidelines (<10 $\mu g/m^3$).[2,6] Given these facts, compelling arguments can be made for implementing strategies to reduce $PM_{2.5}$ levels at both ends of the air pollution severity spectrum worldwide. Unfortunately, economic-political uncertainties along with the burgeoning urban-industrial expansion in many rapidly emerging economies make a significant improvement in global air quality (particularly in highly polluted countries such as India and China) an unlikely near-term reality.

Although the past decade has seen much advancement in our knowledge of how air pollutants promote cardiovascular diseases, important questions remain. The precise nature and systemic pathways, whereby $PM_{2.5}$ elicits a multitude of adverse responses in the heart and vasculature anatomically remote from the site of inhalation, require better elucidation.[3,4] On a more practical note, another commonly posed unresolved question is: what can (and should) an individual do to protect him- or herself against the hazards of air pollution given the fact that substantial improvements in air quality throughout many parts of the world are likely decades away?[3–5]

In this issue, Li et al[7] have provided some significant insights into both of these issues. In a well-designed randomized, double-blind, crossover trial using indoor air purifiers, the investigators demonstrated that short-term exposure (9 days) to high levels of ambient $PM_{2.5}$ (outdoor mean, 101 $\mu g/m^3$) among 55 healthy young students in Shanghai prompted a host of adverse cardiometabolic responses. These responses include increased blood pressure and insulin resistance, as previously shown by us[8] and others, along with alterations in a battery of circulating markers indicative of systemic inflammation, oxidative stress, and platelet activation.[3,4] However, the distinguishing feature of their work from a mechanistic standpoint was the detailed exploration of health responses using state-of-the-art metabolomic profiling. Although similar outcomes after brief exposure to ozone have been shown,[9] this was the first usage of an untargeted metabolomic approach to evaluate the

impact of ambient $PM_{2.5}$. The results confirm and extend the growing body of evidence that $PM_{2.5}$ elicits systemic-wide perturbations favoring the development of the metabolic syndrome.[10,11] Sophisticated analyses of the metabolomic footprints further supported heightened activity of both the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis. As posited by the investigators, the concomitant alterations in blood pressure, insulin sensitivity, and serum metabolites (amino acids, fatty acids, lipids) may have arisen as a direct consequence; yet a contribution by other pathways (eg, generation of secondary oxidation products), as has been postulated by others, cannot be ruled out.[3,4] Additionally, the investigators provided persuasive evidence for the key role of activated central nervous system pathways (eg, increased corticotropin-releasing hormone, adrenocorticotropic hormone, catecholamine precursors) in the etiology of heightened sympathetic nervous system and hypothalamic-pituitary- adrenal axis tone. These observations help to fill a void in our understanding of the complex, overlapping intermediary pathways whereby inhaled $PM_{2.5}$ prompts a wide array of systemic cardiometabolic responses.

How does the inhalation of pollutants activate central nervous system loci resulting in a stress response? One possible explanation is the triggering of afferent nerves originating from the airways and lungs that mediate reflex efferent pathways that modulate systemic effects.[3,4,10,11] It is also possible that nanoparticles and soluble compounds within $PM_{2.5}$ or secondary endogenous biological intermediates, such as oxidized phospholipids, can be transported directly by cranial nerve axons or reach permeable central nervous system sites by the circulation. Our prior animal experiments indeed confirm a pivotal role for hypothalamic inflammation (nuclear factor κB-dependent signaling) in the genesis of peripheral metabolic and hemodynamic abnormalities induced by $PM_{2.5}$ exposure.[10–13]

The findings by Li et al[7] also add to the growing body of evidence that simple interventions such as air purifier systems using high-efficiency particulate arrestance filters can help protect against adverse health impacts of air pollution.[5,13] The reduction in estimated $PM_{2.5}$ exposure afforded by filtration favorably influenced most of the health outcomes (blood pressure, insulin resistance, oxidative stress, inflammation), curtailed $PM_{2.5}$-induced activation of the sympathetic nervous system and hypothalamic-pituitary-adrenal axis, and helped mitigate the ensuing metabolomic perturbations. Although indoor air purification has ostensible merit, the estimated reduction in time-averaged exposure was only 50%, as in prior studies.[5,13] Average $PM_{2.5}$ exposure remained at 24 $\mu g/m^3$ even during air purification, which is 2 to 3 times that faced by most Americans[2] and may leave most people incompletely protected. Thus, more substantial reductions in exposure may be required to optimally protect public health.[5,6] Moreover, this study represents near-ideal scenarios among healthy individuals living in relatively confined indoor spaces. These facts raise additional important questions. Is a 50% reduction in $PM_{2.5}$ exposure even worthwhile from a health standpoint during extremely polluted periods (100–500 $\mu g/m^3$)? Do health benefits of filtration persist over the long term? Would additional personal-protection actions if implemented outdoors during periods of maximal exposure (exercise and commutes) result in further benefits? Last, does reducing $PM_{2.5}$ exposures among at-risk populations, such as patients with cardiovascular disease, translate into actual clinical benefits (eg, prevent future myocardial infarctions)?

One approach to overcome the challenges presented by the indoor-outdoor continuum of high $PM_{2.5}$ exposures in heavily polluted regions is to wear N95 masks while outside. These facemasks block >95% of particle inhalation when fit properly and are more effective than surgical or cloth masks. A few prior studies have shown that N95 respirators can provide cardiovascular protection during outdoor activity in Beijing.[5,13] Indeed, findings by this same group of investigators recently demonstrated favorable changes in blood pressure and other biomarkers when healthy young adults in Shanghai wore N95 respirators.[14] Given the danger posed by air pollution and the short-term benefits of personal-protection strategies (indoor air filtration and N95 facemasks) on improving surrogate health end points, why have these relatively inexpensive practical approaches not been promoted to the public at-large by scientific and health agencies?[3,4] The answer is that there have been no large-scale randomized controlled outcome studies with hard cardiovascular end points (eg, acute coronary syndromes, strokes, heart failure) to conclusively support the basis for any such formal recommendations in any population. As we recently proposed, the time has come for just such a definitive trial (focusing initially on high-risk patients).[15] Prior studies[5,13] and the current results from Li et al[7] have provided the necessary foundation bolstering the scientific plausibility to formally test the benefits of these personal-prevention approaches. We believe clinical outcome trials are now warranted to significantly move this field forward from a scientific and health policy standpoint. The era of simply being stressed about $PM_{2.5}$ without being able to take proven personal-protective actions should come to an end.

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References

1. Narayan KM, Ali MK, Koplan JP. Global noncommunicable diseases: where worlds meet. N Engl J Med. 2010; 363:1196–1198. DOI: 10.1056/NEJMp1002024 [PubMed: 20860499]
2. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, Balakrishnan K, Brunekreef B, Dandona L, Dandona R, Feigin V, Freedman G, Hubbell B, Jobling A, Kan H, Knibbs L, Liu Y, Martin R, Morawska L, Pope CA 3rd, Shin H, Straif K, Shaddick G, Thomas M, van Dingenen R, van Donkelaar A, Vos T, Murray CJL, Forouzanfar MH. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet. 2017; 389:1907–1918. DOI: 10.1016/S0140-6736(17)30505-6 [PubMed: 28408086]
3. Newby DE, Mannucci PM, Tell GS, Baccarelli AA, Brook RD, Donaldson K, Forastiere F, Franchini M, Franco OH, Graham I, Hoek G, Hoffmann B, Hoylaerts MF, Künzli N, Mills N, Pekkanen J, Peters A, Piepoli MF, Rajagopalan S, Storey RF. ESC Working Group on Thrombosis, European Association for Cardiovascular Prevention and Rehabilitation; ESC Heart Failure Association. Expert position paper on air pollution and cardiovascular disease. Eur Heart J. 2015; 36:83b–93b. DOI: 10.1093/eurheartj/ehu458 [PubMed: 25492627]
4. Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC Jr, Whitsel L, Kaufman JD. American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the

American Heart Association. Circulation. 2010; 121:2331–2378. DOI: 10.1161/CIR.0b013e3181dbece1 [PubMed: 20458016]

5. Morishita M, Thompson KC, Brook RD. Understanding air pollution and cardiovascular diseases: is it preventable? Curr Cardiovasc Risk Reports. 2015; 9:1–9.
6. Crouse DL, Peters PA, van Donkelaar A, Goldberg MS, Villeneuve PJ, Brion O, Khan S, Atari DO, Jerrett M, Pope CA, Brauer M, Brook JR, Martin RV, Stieb D, Burnett RT. Risk of nonaccidental and cardiovascular mortality in relation to long-term exposure to low concentrations of fine particulate matter: a Canadian national-level cohort study. Environ Health Perspect. 2012; 120:708–714. DOI: 10.1289/ehp.1104049 [PubMed: 22313724]
7. Li H, Cai J, Chen R, Zhao Z, Ying Z, Wang L, Chen J, Hao K, Kinney PL, Chen H, Kan H. Particulate matter exposure and stress hormone levels: a randomized, double-blind, crossover trial of air purification. Circulation. 2017; 136:618–627. DOI: 10.1161/CIRCULATIONAHA.116.026796 [PubMed: 28808144]
8. Brook RD, Sun Z, Brook JR, Zhao X, Ruan Y, Yan J, Mukherjee B, Rao X, Duan F, Sun L, Liang R, Lian H, Zhang S, Fang Q, Gu D, Sun Q, Fan Z, Rajagopalan S. Extreme air pollution conditions adversely affect blood pressure and insulin resistance: the Air Pollution and Cardiometabolic Disease Study. Hypertension. 2016; 67:77–85. DOI: 10.1161/HYPERTENSIONAHA.115.06237 [PubMed: 26573709]
9. Rajagopalan S, Brook RD. Ozone-induced metabolic effects in humans: ieiunium, conviviorum, aut timor? (fasting, feasting, or fear?). Am J Respir Crit Care Med. 2016; 193:1327–1329. DOI: 10.1164/rccm.201601-0142ED [PubMed: 27304238]
10. Rao X, Patel P, Puett R, Rajagopalan S. Air pollution as a risk factor for type 2 diabetes. Toxicol Sci. 2015; 143:231–241. DOI: 10.1093/toxsci/kfu250 [PubMed: 25628401]
11. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook FR, Chen LC, Brook RD, Rajagopalan S. Environmental stressors and cardio-metabolic disease: part II: mechanistic insights. Eur Heart J. 2017; 38:557–564. DOI: 10.1093/eurheartj/ehw294 [PubMed: 27460891]
12. Liu C, Fonken LK, Wang A, Maiseyeu A, Bai Y, Wang TY, Maurya S, Ko YA, Periasamy M, Dvonch T, Morishita M, Brook RD, Harkema J, Ying Z, Mukherjee B, Sun Q, Nelson RJ, Rajagopalan S. Central IKKβ inhibition prevents air pollution mediated peripheral inflammation and exaggeration of type II diabetes. Part Fibre Toxicol. 2014; 11:53.doi: 10.1186/s12989-014-0053-5 [PubMed: 25358444]
13. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen LC, Brook RD, Rajagopalan S. Environmental stressors and cardio-metabolic disease: part I: epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. Eur Heart J. 2017; 38:550–556. DOI: 10.1093/eurheartj/ehw269 [PubMed: 27460892]
14. Shi J, Lin Z, Chen R, Wang C, Yang C, Cai J, Lin J, Xu X, Ross JA, Zhao Z, Kan H. Cardiovascular benefits of wearing particulate-filtering respirators: a randomized crossover trial. Environ Health Perspect. 2017; 125:175–180. DOI: 10.1289/EHP73 [PubMed: 27562361]
15. Brook RD, Newby DE, Rajagopalan S. The global threat of outdoor ambient air pollution to cardiovascular health: time for intervention. JAMA Cardiol. 2017; 2:353–354. DOI: 10.1001/jamacardio.2017.0032 [PubMed: 28241232]